

REMARKS

The withdrawal of objections and rejections in the prior Office Action as set forth by the Examiner on page 2 of the current Office Action is acknowledged.

The specification is objected to in view of gaps and blank segments on pages 43, 50, 54, 96 and 130. This objection is traversed. It is noted that the gaps and blank segments do not include numbered lines in the margin and therefore indicate that no subject matter was intended to be present. Consequently, it is Applicants' understanding that at the time an allowed patent would be printed, all such gaps and blank segments would no longer be present in the conformed document. However, if the Examiner so requires, and at such time as allowable claims are indicated, Applicants are prepared to file a substitute specification with all identified gaps and blank segments removed.

Claims 1-25, 27 and 36 are rejected under 35 U.S.C. § 112, first paragraph, "because the specification, while being enabling for, compounds in Tables 1-4 (compounds 1-133, pages 26-29, 136-159) does not reasonably provide enablement for all the compounds presented by the general structure formula (I) of claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use or make the invention commensurate in scope with these claims." (Office Action, page 3) This rejection is traversed.

In support of the rejection, the Examiner reviews various aspects of the decision *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). In particular, the Examiner reviews the so-called *Wands* factors 1-8 on pages 4-8 of the Office Action. For convenience, these factors will be similarly referred to by number and comments will be provided in response to the Examiner's remarks.

The first factor, "the breadth of the claims", is stated by the Examiner to be presented by the general structure formula (I) of claim 1. The second factor, "the nature of the invention", is said to be "a novel class of pharmaceutical compounds that are inhibitors of Hepatitis C Virus (HCV) protease activity, specifically compounds that inhibit HCV NS3/NS4a serine protease activity." With regard to "the state of prior art" (factor 3), the Examiner acknowledges that, with regard to the general structure formula (I) of claim 1, the prior art does not provide any evidence of HCV protease inhibitory activity, specifically with regard to HCV NS3/NS4a serine protease inhibitory activity. The Examiner states that "the relative skill in the art" (factor 4) as it relates to the subject pharmaceutical compounds, is that of "a M.D. or Ph. D. level individual." Applicants take no exception to the Examiner's summary of *Wands* factors 1-4 as set forth above.

In discussing the "level of predictability in the art," the Examiner states "since the prior art does not teach that the compounds presented by general formula (I) of claim 1 formerly existed, the level of predictability is low in regards to the compounds of the invention with respect to HCV serine protease inhibitory activity." The Examiner concludes "Therefore, one of skill in the art would not be able to readily anticipate the inhibitory effects of the compounds of the invention." (Office Action, page 6) While apparently reasonable on its face, the Examiner's conclusion with regard to predictability does not take into consideration Applicants' own teachings. While Applicants' teachings may be considered under the heading of *Wands* factor 6 (the amount of guidance present), characterizing the level of predictability as being "low" suggests that one of skill in the art would be burdened when faced with a determination of whether or not a compound within the scope of formula (I) of claim 1 would have the requisite

inhibitory activity. Contrary to the Examiner's view, having read Applicants' full disclosure, one of skill in the art will have learned that the compounds within the scope of general formula (I) of claim 1 have been demonstrated to exhibit the requisite inhibitory activity and, therefore, one of skill in the art would expect that such compounds will "predictably" have the desired response. Consequently, while the prior art is lacking with regard to a teaching sufficient to allow prediction of the performance of the compounds of formula (I) of claim 1, Applicants' teachings provide the necessary further knowledge that will allow one of skill in the art to predict the performance of the claimed compounds, or at least to expect that such compounds will perform satisfactorily as claimed.

With regard to the "amount of guidance present" (*Wands* factor 6), the Examiner states "The Applicants have not provided guidance for all the compounds presented in the general formula (I) of claim 1." (Office Action, page 6; emphasis supplied) By means of this characterization, the Examiner implies that Applicants must present results for all of the compounds of general formula (I) of claim 1. In contrast, if the Examiner is merely suggesting that Applicants should provide guidance sufficient to apply to all of the compounds presented in the general formula (I) of claim 1, it is respectfully suggested that Applicants have explicitly done so.

The operative word in *Wands* factor 6 is "guidance." In Tables 1 and 4 of the application, Applicants provide specific performance for 149 compounds with regard to inhibitory activity of compounds within the claimed scope. Were this not enough, Applicants further provide, beginning on page 130 and continuing through page 135, explicit details of the methods required to assay for HCV protease inhibitory activity according to methods well-known to those skilled in the art to which the invention pertains. Applicants identify the specific references

which were employed as well as an explanation of the means by which they employed the referenced techniques to their claimed invention. As stated *In re Wands*, "*Wands*' disclosure provides considerable direction and guidance on how to practice their invention and presents working examples. There was a high level of skill in the art at the time when the application was filed, and all of the methods needed to practice the invention were well known." (*Id.*, 1406) Clearly, as evidenced by the referenced pages above, the same facts and circumstances apply to the presently claimed invention.

Furthermore, while the Examiner notes that there is a "wide range of Ki values that is associated with these compounds" (Office Action, page 6), Applicants teach that this range has "excellent utility as NS3-serine protease inhibitors" (page 135, lines 13-17).

Additionally, the Examiner comments that it would be difficult for a person of skill in the art to be able to use the correct amount of compound of the invention since "Applicants have only shown how to make a "limited number" of peptides of the invention, compounds 1-133 (examples 1-20), since the general structure formula of claim 1 allows for a much larger number of possible peptides than disclosed, a person of skill in the art would need more guidance as to how to make all of the compounds presented by the general structure formula of claim 1." (Office Action, page 7, emphasis supplied)

Respectfully, these comments confound two different issues with regard to the claimed invention. First, Applicants have provided specific teachings by which those of skill in the art (recalling that such persons have either a Ph. D. or a medical degree) for determining the activity of a particular compound and to adjust the amount required so that such a compound will be useful for effecting the necessary protease inhibitory activity. Furthermore, the general preparative

schemes and synthesis schemes detailed in the application (starting at page 41 and continuing through page 131) and also including application of the synthesis schemes to specific syntheses, such disclosures clearly demonstrate how to make a wide array of compounds within the claimed scope; certainly, highly skilled persons such as a Ph. D. or M.D. would be capable of applying Applicants' comprehensive teachings. The Examiner has provided no basis on which to conclude that the teachings of the application would not be generally applicable to all compounds within the scope of the claims, whereas Applicants have clearly demonstrated that their synthesis methods and screening techniques, set forth in detail in the application and in the art, are generally applicable to compounds within the full scope of the claims.

Further in this regard, and under the title relating to "the existence of working examples" (*Wands* factor 7), the Examiner states that the "specification does not provide working examples of all compounds suggested by the general structure formula (I) of claim 1." (Office Action, page 7, emphasis supplied) Contrary to the Examiner's view, the law does not require working examples of all compounds suggested by a claimed generic structure. In fact, the *Wands* decision sets forth a series of factors to be considered, and also as presented and discussed by the Examiner, explicitly because experimental evidence is not required for all compounds claimed by an inventor.

Finally, with regard to *Wands* factor 8, "the quantity of experimentation necessary", the Examiner has focused on "using all the compounds suggested by the general structure formula (I) of claim 1." However, by presenting experimental evidence relating to a determination of *Ki*, Applicants have presented a significant amount of experimental evidence regarding the inhibitory activity of the claimed compounds and,

therefore, how such compounds are to be used. In other words, given that a compound inhibits HCV NS3 serine protease, one of skill in the art would expect it to have the requisite utility in the treatment of HCV. Furthermore, Applicants have clearly set forth several synthesis schemes and evaluation methods (as described in the prior art) for both making and using the claimed compounds.

Consequently, although such synthesis and testing methods may be complex, they are, in view of the comprehensive teachings of the application, and with reference to methods known in the art, merely routine and certainly within the skill of one in the art. As observed *In re Wands*, "the test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." (*Id.* 1404) It is respectfully suggested that, especially in view of *In re Wands*, Applicants are entitled to the full scope of the claims as set forth by the general structure formula (I) of claim 1. Withdrawal of the rejection of the claims is respectfully requested.

As it is believed that all of the rejections set forth in the Official Action have been fully met, favorable reconsideration and allowance are earnestly solicited.

If, however, for any reason the Examiner does not believe that such action can be taken at this time, it is respectfully requested that he telephone Applicants' attorney at (908) 654-5000 in order to overcome any additional objections which he might have.

Application No.: 09/909,012

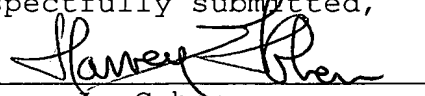
Docket No.: IN01158K

If there are any additional charges in connection with this response, the Examiner is authorized to charge Deposit Account No. 12-1095 therefor.

Dated: November 19, 2004

Respectfully submitted,

By



Harvey L. Cohen

Registration No.: 28,365

LERNER, DAVID, LITTENBERG,

KRUMHOLZ & MENTLIK, LLP

600 South Avenue West

Westfield, New Jersey 07090

(908) 654-5000

Attorney for Applicant

LD-447\